

TO: DONNIE PHOENIX

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QIC TO  
RWT/VR  
J. [Signature]Description of Figures 8A-8J and 9A-9DU.S. Application No. 09/320,299

*6/16/04 D*

Figs. 8A, 8B, and 8C. Phenotypic Drug Susceptibility and Resistance Profile: Patients 302. This is one example of the third pattern of NNRTI susceptibility/resistance. Phenotypic analysis of the patient virus demonstrated reduced susceptibility to both delavirdine and nevirapine. This pattern is characterized by a larger reduction of nevirapine susceptibility compared to the reduction of delavirdine susceptibility. Genotypic analysis of the patient virus demonstrated the presence of the RT mutations K103N associated with nevirapine and delavirdine resistance and P225H.

Figs. 8D, 8E, and 8F. Phenotypic Drug Susceptibility and Resistance Profile: Patients 780. This is a second example of the third pattern of NNRTI susceptibility/resistance. Phenotypic analysis of the patient virus demonstrated reduced susceptibility to both delavirdine and nevirapine. This pattern is characterized by a larger reduction of nevirapine susceptibility compared to the reduction of delavirdine susceptibility. Genotypic analysis of the patient virus demonstrated the presence of the RT mutations K103N associated with nevirapine and delavirdine resistance and P225H.

Fig. 8G. Phenotypic Drug Susceptibility and Resistance Profile: Individual Virus Clones of Patient 302. Genotypic analysis of individual virus clones from patient 302 revealed viruses containing the K103N mutation without the P225H mutation (K103N, I135M, R211K) and viruses containing the K103N mutation with the P225H mutation (K103N, P225H). Phenotypic characterization of these virus clones indicates that the P225H mutation reduces the amount delavirdine resistance associated with the K103N mutation (compare bottom panels), but does not alter the amount of nevirapine resistance associated with the K103N mutation (compare top panels).

Figs. 8H, 8I, and 8J. Phenotypic Drug Susceptibility and Resistance Profile: Site Directed Reverse Transcriptase Mutants. Phenotypic characterization of a virus containing the site directed RT mutation P225H indicates that this mutation increases susceptibility to delavirdine, but not nevirapine (compare top panels). Phenotypic characterization of a virus containing the site directed RT mutations P225H plus K013N or P225H plus Y181C indicate that the P225H mutation decreases the amount of delavirdine resistance associated with either K103N

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or Y181C, but does not decrease the amount of nevirapine resistance associated with K103N or Y181C. to delavirdine, but not nevirapine (compare corresponding middle and bottom panels).

Figs. 9A, 9B, and 9C. Phenotypic Drug Susceptibility and Resistance Profile: Patients 644. This is one example of the fourth pattern of NNRTI susceptibility and resistance. Phenotypic analysis of the patient virus demonstrated by a large reduction in susceptibility to nevirapine, but not delavirdine. Genotypic analysis of the patient virus demonstrated the presence of the RT mutations G190S, as well as the K101E mutation associated with reductions in susceptibility to atevirdine, DMP266, L-697,661 and UC-10,38,57 (Schinazi, Mellors, Larder resistance table).

Fig. 9D. Phenotypic Drug Susceptibility and Resistance Profile: Site Directed Reverse Transcriptase Mutants. Phenotypic characterizations of viruses containing either site directed RT mutations G190A, or G190S indicate that these mutations greatly reduce susceptibility to nevirapine, and slightly increase susceptibility to delavirdine (compare top panels).